

Localized nasal cavity, sinus, and massive bilateral orbital involvement by human T cell leukemia virus 1 adult T cell lymphoma, with epidermal hypertrophy due to mite infestation

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Abstract

HTLV1 adult T cell lymphoma occurs tends to be widely disseminated and aggressive, with only brief responses to chemotherapy. Aside from cervical adenopathy, involvement of head and neck structures is uncommon and orbital involvement rare.

We report a case of nasal cavity HTLV lymphoma with massive bilateral orbital involvement and proptosis, resulting in complete left and partial right eye amaurosis. No other sites of disease were found. Response to chemotherapy was rapid and complete, with almost complete restoration of vision and oculo-motor function; the patient has remained in remission for one year. An associated problem was striking bilateral hypertrophic, hyperkeratotic eyelid and breast lesions due to mite infestation.

Case Report

A 48 year old, previously healthy woman noted bilateral, progressive eyelid swelling in Grenada which proved unresponsive to eye drops prescribed there. This was associated with loss of vision in both eyes. At least a year earlier she had noted cutaneous lesions on her left breasts. Approximately two months after these problems developed she presented to the Kings County Hospital Medical Center.

She was a thin woman with some temporal wasting. There was bilateral conjunctival edema, massive on the left, with proptosis. She was blind in the left eye, with marked visual loss on the right. Both upper eyelids were hypertrophied with extensive hyperkeratotic epidermis lesions.

(Figure 1) Massive, confluent lesions of the same type were noted on her breasts. There was no adenopathy or organomegaly.

Complete blood count was normal, with no abnormal lymphocytes, such as flower or Sezary cells on the blood smear. Calcium was 10.1, albumin 3.9, LDH 280. HTLV1 serology was positive. Chest x-ray and abdominal-pelvic computer-automated tomography revealed no adenopathy. Gd-enhanced magnetic resonance imaging of the head revealed a large mass involving the upper nasal cavity, ethmoid sinuses, with extensive orbital invasion, greater on the left, with optic nerve encasement (Figure 2). The left sphenoid and bilateral frontal sinuses were obstructed, and the superior aspect of the right maxillary sinus was involved. The left orbital mass was 6.3×4.1×3.3 cm; the right medial retrobulbar fat was involved. There was no intracranial extension but bone erosion was suggested. Body computer-automated tomography revealed no other disease.

A biopsy of the left orbital mass by Ophthalmology demonstrated large, highly pleomorphic, and hyperchromatic cells infiltrate. Immunohistochemical studies revealed tumor cells positive for CD45, CD3, CD45, CD45RO, and CD20, but negative for CD79a, CD56, CD30, CD15, TDT, ALK1, Bcl6, Bcl2, CD10, S-100, AE1/AE3, synaptophysin, and Chromogranin. (Figure 3A-F). The final diagnosis was peripheral T cell lymphoma with aberrant expression of CD20. Eyelid biopsy was negative for lymphoma, but revealed large clusters of Norwegian scabies (*Sarcoptes scabiei var. hominis*) (Figure 4A-B).

She was started on the EPOCH regimen, consisting of continuous infusions of etoposide 50 mg/m², vincristine 0.4 mg/m², doxorubicin 10 mg/m² days 1-4, cyclophosphamide 750 mg/m² day 5, prednisone 60 mg/m² days 1-5, and rituximab. Response was rapid and complete after 6 cycles; her chemosis subsided (Figure 5) and vision was restored to both eyes, though a partial left lateral rectus palsy persisted. The eyelid and breast cutaneous lesions did not subside with chemotherapy, but resolved completely with oral ivermectin therapy. She remains in complete remission 1 year after initiation of chemotherapy. Nine months later flow cytometry of an apparently normal peripheral blood specimen revealed 2.4 CD25⁺ cells/mm³.

Discussion

There is only one previous report of orbital involvement by HTLV1 lymphoma,¹ in a patient with acute ATLL. Primary involvement of the globe by HTLV1 cells has been described, often associated with local opportunistic infection. A patient of our own with ATLL leukemia developed frosted branch retinopathy which was found, on vitreous biopsy, to be due to leukemic cells and

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Figure 1. Hypertrophied upper eye lids.



Figure 2. Computed tomography depicting encasement of optic nerve by tumor.

herpes simplex 2 infection. Our patient's extraordinarily destructive orbital implants may have arisen from a primary lesion in her nasal cavity. Her severe complications are in contrast to the results of low grade B lymphomatous involvement of this region. Waldeyer's ring and sinus involvement may occur in disseminated HTLV1 lymphomas, but a syndrome of primary involvement of these regions in 6 patients has been described.² As in our patient, these tumors were destructive but localized, and 5 of the 6 patients survived relapse-free for 27-78 months (median 44, mean 49) after chemotherapy. This contrasts with the early relapses usually observed after the response of disseminated HTLV1 lymphomas to chemotherapy.

The expression of CD20, a B cell marker, by our patient's tumor cells is rare in HTLV1 lymphoma, though previously reported.^{3,4} There is

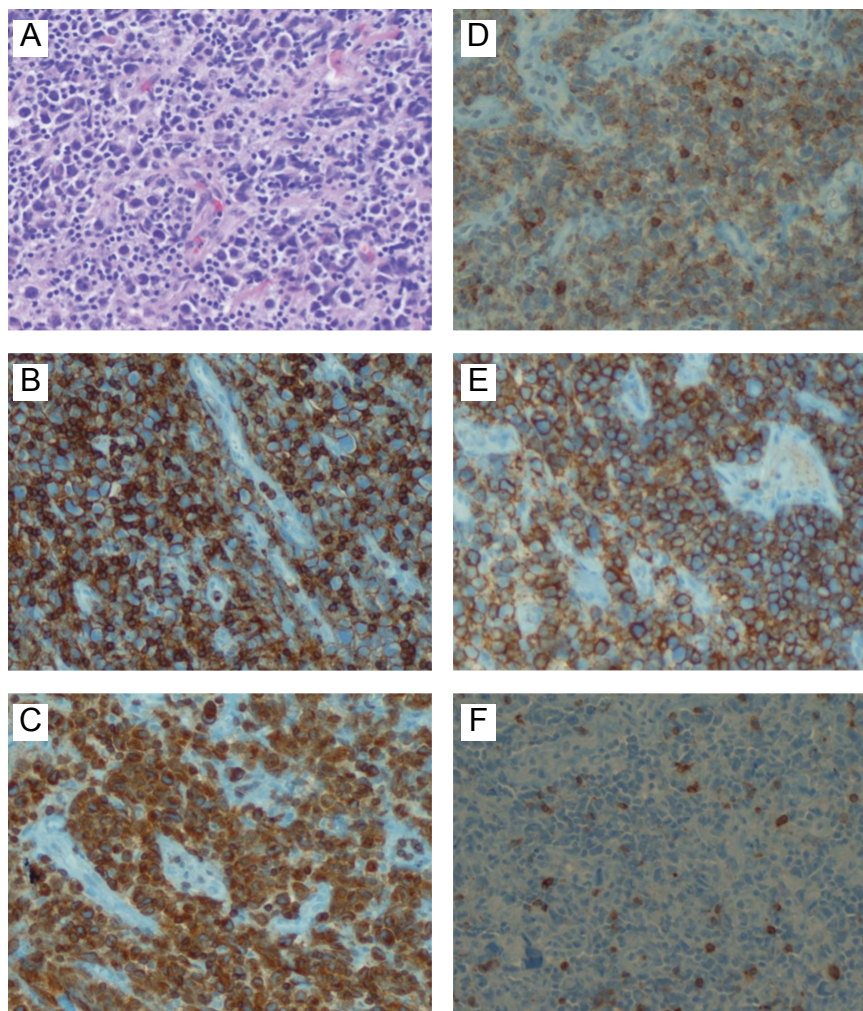


Figure 3. (A) Biopsy showed large, highly pleomorphic, and hyperchromatic cells infiltrates. Hemotoxylin-Eosin stain @ 200x magnification. Immunohistochemical studies performed on paraffin sections at 200x magnification: (B) CD 45 (C) CD3 (D) CD45RO (E) CD20 (F) CD79a

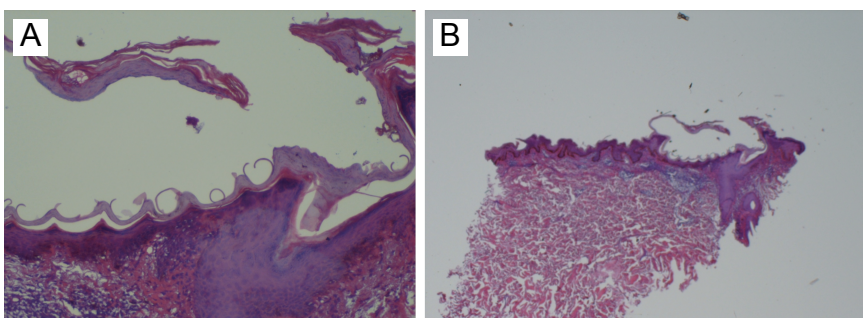


Figure 4. Skin biopsy taken from patient revealing mite infestation.

no evidence that it occurs in other HTLV1 tumors of the head region. The orbital biopsy specimen was too small for studies of the viral genome, or T and B cell clonality. But the following data support the diagnosis of an HTLV1-related T cell lymphoma: i) All tumor cells were CD3⁺; ii) All were CD79a negative; iii) Our patient's cutaneous mite infestation is specific

to HTLV1 lymphomas; vi) There was a high level of circulating CD25⁺ cells in the remission blood specimen. The pathogenesis of the syndrome of localized and highly responsive HTLV1 lymphomatous involvement of head structures is not clear. It may be due to a population of lymphoma cells whose ability to proliferate is restricted to this region. Extirpation of this cell



Figure 5. Picture of patient's eyelids after treatment revealing almost complete resolution as compared to initial presentation.

population may therefore be curative. Our and others' data² suggests that aggressive HTLV1 lymphomatous involvement of head structures other than lymph nodes may be localized, and completely and durably responsive to chemotherapy. It may represent a separate subtype of HTLV1 lymphoma, in that it is systemically smoldering or subclinical, but locally aggressive. Gross cutaneous mite infestation has been reported in other patients with HTLV1 lymphomas,⁵ though we have not observed it in several hundred patients of Caribbean origin with HTLV1 lymphomas at our institution. HTLV1 lymphomas often involve the skin, but do not cause hyperkeratosis. It is therefore important to biopsy such lesions. Opportunistic mite infestation has not been reported in association with other lymphomas or with immune deficiency. The basis of HTLV1 patients' specific susceptibility to mite infestation is not known. Eyelid edema caused by obstruction of lymphatic drainage by orbital tumors and secondary proptosis may have facilitated extensive mite infestation of the eyelids. But no mites were found in the orbital biopsy, which suggests that they did not contribute to her proptosis.

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